IN THE SPECIFICATION:

Please replace the paragraph on page 1, lines 3-4, with the following rewritten paragraph:

This filing is a divisional of commonly assigned, co-pending application 09/970,446, filed October 3, 2001, which ~~patent application~~ claims benefit of U.S. provisional patent application No. 60/239,023, filed October 4, 2000, each of which is incorporated by reference.

Please replace the paragraph on page 6, lines 9-31, with the following rewritten paragraph:

Glucocorticoids (GC), including ~~Dexamethazone~~ Dexamethasone (Dex), are potent antiinflammatory and immunosuppressive agents that are widely used in the treatment of inflammatory disorders, such as autoimmune and allergic diseases (~~Wilkens and de~~ Wilckens and ~~de~~ De Rijk (1997) Immunol. Today 18:418-424; Schleimer, et al. ~~(ed. 1997)~~ (eds.) (1997) Inhaled Glucocorticoids in Asthma: Mechanisms & Clinical Actions, Marcel Dekker, NY, NY. GC have been shown to have an inhibitory effect on both T cells and APC, at the level of proliferation as well as cytokine production, with down-regulation of IFN-γ, IL-4, and IL-5 under some conditions, but upregulation of IL-4 under other conditions. See Blotta, et al. (1997) J. Immunol. 158:5589-5595; Ramirez, et al. (1996) J. Immunol. 156:2406-2412; and Daynes and Araneo (1989) Eur. J. Immunol. 19:2319-2325. This may result from indirect effects, e.g., GC down-regulate the production of IL-12 by APC and thus IFN-γ production by T cells (Blotta, et al. (1997) J. Immunol. 158:5589-5595; Vieira, et al. (1998) J. Immunol. 161:5245-5251; and Visser, et al. (1998) Blood 91:4255-4264), and thus in some cases may indirectly upregulate the production of IL-4 (Blotta, et al. (1997) J. Immunol. 158:5589-5595) and or IL-5 (Vieira, et al. (1998) J. Immunol. 161:5245-5251) and/or IL-10 (Vieira, et al. (1998) J. Immunol. 161:5245-5251; and Visser, et al. (1998) Blood 91:4255-4264) in cultures contain APC, antigen, and T cells. Recently, it has been shown that GC drive human CD8+ T cell differentiation towards a stable

phenotype with high IL-10 and reduced IFN-γ, IL-4, IL-5 and IL-13 production. See Richards ~~and Hawrylowicz~~ , et al. (2000) Eur. J. Immunol. 30:2344-2354.

Please replace the paragraph beginning on page 6, line 32, and continuing to page 7, line 12, with the following rewritten paragraph:

GC bind the cytosolic GC receptor (GR), which then translocates to the nucleus and inhibits the transcriptional activation of target genes. See review of Karin, in Schleimer, et al. ~~(ed. 1997)~~ ,supra ~~Inhaled Glucocorticoids in Asthma: Mechanisms & Clinical Actions Dekker~~; and Karin (1998) Cell 93:487-490. GC mediate transcriptional repression through: 1) interfering with the function of transacting factors, such as AP-1 and NFκB (De Bosscher, et al. (1997) Proc. Nat'l. Acad. Sci. USA 94:13504-13509), via protein-protein interactions; and inhibition of NFAT binding to cytokine gene promoters (Chen, et al. (2000) J. Immunol. 164:825-832); 2) direct DNA binding to poorly conserved negative GC responsive elements (GRE); or 3) inducing the expression of inhibitory factors such as IkBa (reviewed in Karin in Schleimer, et al., supra ~~(eds. 1997) Inhaled Glucocorticoids in Asthma: Mechanisms & Clinical Actions Dekker)~~. Furthermore, GR represses TGF-β transcriptional activation of the plasminogen activator PAI-1 gene in a ligand-dependent manner, by both Smad3 and Smad4 C-terminal activation domains. See Song, et al. (1999) Proc. Nat'l Acad. Sci. USA 96:11776-11781.

Please replace the paragraph beginning on page 7, line 28, and continuing to page 8, line 10, with the following rewritten paragraph:

~~1,25(OH)-dihydroxyvitamin D3~~ 1,25(OH)-Dihydroxyvitamin D3 (VitD3) is a secosteroid receptor hormone that binds to a nuclear receptor named Vitamin D3 receptor (VDR). Once bound to the hormone ligand the receptor associates with specific recognition sequences called vitamin D responsive elements (VDRE) which are present in the promoter regions of target genes and are involved in regulating their transcription. Recent studies have shown that VitD3 represses IL-2 gene transcription by VDR-dependent inhibition of NFATp/AP-1 complex formation. Alroy, et al. (1995)

Mol. Cell Biol. 15:5789-5799. In addition, it has also been reported that VitD3 mediates downregulation of NF-kB activation by decreasing NF-kB p50 and c-Rel expression in T cells. Yu, et al. (1995) Proc. Nat'l Acad. Sci. USA 92:10990-10994. The inhibition of transcription activation of the IL-12 p35 and p40 genes by VitD3 may be, in part, by downregulation of NF-kB activation and binding to the p40-kB sequence. D'Ambrosio, et al. (1998) J. Clin. Invest. 101:252-262. In addition, SMAD3, one of the SMAD proteins downstream in the TGF-β signaling pathway, which was inhibited by GC, acts as a coactivator specific for ligand-induced transactivation of VDR. ~~Yanigisawa~~ Yanagisawa, et al. (1999) Science ~~286~~ 283:1317-1321.

Please replace the paragraph on page 12, lines 17-26, with the following rewritten paragraph:

Stimulation of ~~naïve~~ naive T cells (CD4+CD62L+) using Antigen Presenting Cells (APC) in the presence of VIT D3 and DEX gives rise to: about 60% IL-10 positive cells (producing at least 500 ng of IL-10 per 106 cells); about 10% IL-10 and IL-4 double positive cells (producing about 50 ng of IL-4 per 106 cells); less than about 1% IL-5 positive cells (producing less than about 30 pg of IL-5 per 106 cells); and less than about 5% IFN-γ positive cells (producing less than about 40 ng of IFN-γ per 106 cells). The cytokine profiles produced by the cells after restimulation are evaluated after 6 h by FACS analysis, while the quantities are accumulated by the respective cell population in 1 ml for 48 h.

Please replace the paragraph on page 12, lines 27-35, with the following rewritten paragraph:

Alternatively, stimulation of ~~naïve~~ naive T cells using Antigen Presenting Cells (APC) in the presence of VitD3 and Dex + anti-IL-4 + anti-IL-12 + anti-IFN-γ gives rise to a population of cells: about 25-35% IL-10 positive cells (producing at least about 100 ng of IL-10 per 106 cells); less than about 1% IL-4 positive cells (producing about 30-1000 pg of IL-4 per 106 cells); less than about 1% IL-5 positive cells (producing less than about 30 pg of IL-5 per 106 cells); less than about 1% IFN-γ positive cells (producing less than about 30 pg of IFN-γ per 106 cells); and less than about 5% IL-2 positive cells (producing about 30-350 pg IL-2 per 106 cells).

Please replace the paragraph on page 13, lines 1-7, with the following rewritten paragraph:

If the stimulation of ~~naïve~~ naive T cells is performed in the presence of anti-CD3 + anti-CD28 with VitD3 and Dex, the resulting population of cells is: about 70-75% IL-10 positive cells; less than about 2% IL-4 positive cells; less than about 1% IL-5 positive cells; less than about 1% IFN-γ positive cells; and less than about 2% IL-2 positive cells. Corresponding quantities of cytokines should be detected according to the cell types described immediately above.

Please replace the paragraph on page 13, lines 8-12, with the following rewritten paragraph:

Stimulation of ~~naïve~~ naive T cells using anti-CD3 + anti-CD28 in the presence of VitD3 and Dex + anti-IL-4 + anti-IL-12 + anti-IFN-γ gives rise to a population of: about 60% IL-10 positive cells; less than about 1% IL-4 positive cells; less than about 1% IL-5 positive cells; less than about 1% IFN-γ positive cells; and about 10% IL-2 and IL-10 double positive cells.

Please replace the paragraph on page 13, lines 13-24, with the following rewritten paragraph:

This data on the development of IL-10 only producing cells using Vitamin D3 and Dexamethazone plus antigenic stimulation of CD4+ T cells has also been reproduced in human systems. In this case there is some dependency on IL-4. Stimulation of purified human ~~naïve~~ naive T cells from cord-blood (CD4+CD45RA+) using L cells (expressing CD32, CD86) as APC plus anti-CD3 in the presence of VitD3 and Dex gives rise after one week of stimulation to a majority of IL-10 producing T cells: VitD3 is used at 2 x 10-8 M (2 x 10-9 M to 2 x 10-7 M) while Dex is used at 10-7 M (10-8 M to 10-6 M). In addition, stimulation of purified ~~naïve~~ naive T cells enriched from human peripheral blood (CD4+CD45RA+) using anti-CD3/+/- anti-CD28, in the presence of VitD3 and Dex gives rise after one week of stimulation to a majority of IL-10 producing T cells.

Please replace the paragraph beginning on page 24, line 30, and continuing to page 25, page 16, with the following rewritten paragraph:

Peripheral blood mononuclear cells (PBMC) were isolated from peripheral blood, freshly collected into sodium citrate, by centrifugation on a Lymphoprep ® (Nycomed, Birmingham, UK) density gradient. Donors were healthy at the time of the study. PBMC were positively selected for CD8+ or CD4+ T cells using antibody-coated magnetic beads and Detach-a-beads ® (Dynal (UK), Wirral, GB) according to the manufacturer's guidelines. Alternatively, PBMC were depleted of CD4+ or CD8+ T cells by negative selection using antibody-conjugated magnetic beads to give CD8+ APC or CD4+ APC populations, respectively. CD4+ T cells were further subdivided into ~~naïve~~ naive CD45RA+ and antigen-experienced CD45RO+ populations using specific antibodies (PharMingen, San Diego, CA) and negative selection with magnetic beads. APC consisted predominantly of CD4low, CD14+ monocytes (13-28%), although a minor population (1.3-5%) of CD4low, CD14- cells is likely to contain DC. Isolated populations were washed and resuspended at 1 x 10^6/ml in RPMI 1640 (Life Sciences, Abingdon, GB) containing 10% heat-inactivated ~~FCS~~ fetal calf serum (FCS) (PAA Laboratories, Oxford, GB), 2 mM L-glutamine, and 50 µg/ml gentamycin (both from Life Sciences). Cell purity was assessed by flow cytometry using a FACScan ® (Becton

Dickinson, Abingdon, GB) and Lysis 2 software. Anti-CD4 (Leu-3a) and CD14 (Leu-M3) antibodies were purchased from Becton Dickinson; CD3 (UCHT1), CD8 (UCHT4), isotype-matched control IgG1 (MOPC21), and IgG2b (MOPC141) antibodies were from Sigma (Poole, GB).